DA $ ZW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/776,037	Confirmation No.: 1520
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	February 9, 2004	
Title	:	Methods and Kits for Locally Administering an Active Agent to an Interstitial Space for a Host	
Group Art Unit	:	1636	
Examiner	:	N/A	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.47(A)

[COVER LETTER / TRANSMITTAL]

Sir:

1. DOCUMENTS ENCLOSED:

In response to the **DECISION ON PETITION UNDER 37 C.F.R. 1.47(A)**, which was mailed by the Patent Office on May 6, 2005, enclosed are:

☒ [Renewed] Petition Under 37 C.F.R. § 1.47(A)

☒ Supplemental Declaration of Facts in Support of Filing on Behalf of Unavailable Inventors (37 C.F.R. § 1.47(A))

06/20/2005 MAHMED1 00000057 150665 10776037

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CERTIFICATE OF MAILING
37 CFR §1.8

I hereby certify, pursuant to 37 CFR §1.8, that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) would be mailed or transmitted on or before the date indicated with the United States Postal Service with sufficient postage as first class mail on the date shown below in an envelope addressed to Mail Stop Missing Parts, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: June 15, 2005

Valerie Cloyd

Applicant	:	Yock, et al.
Appl. No.	:	10/776,097
Examiner	:	N/A
Docket No.	:	13854.4004

2. FILING FEES

☒ Applicant claims small entity status pursuant to 37 CFR 1.27.

BASIC FILING FEE:						$0.00
Total Claims		- 20 =		x	$18.00	$ 0.00
Independent Claims		- 3 =	0	x	$86.00	$0.00
Multiple Dependent Claims	$290	(if applicable)☐				$0.00
Surcharge 37 CFR § 1.16(e)		(if applicable)☒				
TOTAL OF ABOVE CALCULATIONS						$0.00
Reduction by ½ for Filing by Small Entity. Note 37 CFR §§ 1.9, 1.27, 1.28. ☒						$0.00
Extension of Time (from above)						$0.00
Petition Fee (1.17(h)) ☒						$130.00
TOTAL FEES SUBMITTED HEREWITH						$130.00

3. Method of Payment of fees:

☐ A check in the amount of $_____ is enclosed to cover the above fee(s).

☒ Charge Orrick's Deposit Account No. **15-0665** in the amount of **$130.00**.

☐ The Commissioner is authorized to charge Orrick's Deposit Account No. **15-0665** for any fees required under 37 CFR § 1.17 that are not covered, in whole or in part, by a check enclosed herewith and to credit any overpayments to said Deposit Account No. **15-0665**.

Respectfully submitted,

ORRICK, HERRINGTON & SUTCLIFFE LLP

Dated: June 15, 2005

By: _____

Charles C. Fowler
Reg. No. 39,675

Orrick, Herrington & Sutcliffe LLP
4 Park Plaza, Suite 1600
Irvine, CA 92614-2558
Tel. 949-567-6700
Fax: 949-567-6710
Customer Number: 34313

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/776,037	Confirmation No.: 1520
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	February 9, 2004	
Title	:	Methods and Kits for Locally Administering an Active Agent to an Interstitial Space of a Host	
Group Art Unit	:	1636	
Examiner	:	not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

[RENEWED] PETITION UNDER 37 C.F.R. § 1.47(A)

Sir:

This Renewed Petition under 37 C.F.R. § 1.47(a) is being filed in response to the Decision denying Applicants' prior petition, which Decision is stamped as having been mailed by the Office of Petitions on May 6, 2005 (hereinafter referred to as "the Decision"). The Decision invited this reply to be filed within two months from the mailing date of the Decision. Thus, this Renewed Petition is timely filed.

This Renewed Petition is accompanied by the enclosed "Supplemental Declaration of Facts in Support of Filing on Behalf of Unavailable Inventors (37 C.F.R. § 1.47(A))" (hereinafter "the Supplemental Declaration"). The Supplemental Declaration is believed to be in compliance with the requests for additional information set forth in the Decision, and is in full compliance with 37 C.F.R. § 1.47(a) and section 409.03(d) of

CERTIFICATE OF MAILING
37 CFR §1.8

I hereby certify, pursuant to 37 CFR §1.8, that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) would be mailed or transmitted on or before the date indicated with the United States Postal Service with sufficient postage as first class mail on the date shown below in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Dated: June 15, 2005

Valerie M. Cloyd

the M.P.E.P. Applicants respectfully request prompt and favorable treatment of this Renewed Petition.

The Commissioner is hereby authorized and requested to charge Orrick's Deposit Account No. 15-0665 in the amount of $130.00 for the Petition Fee required under 37 CFR § 1.17(h).

Respectfully submitted,
ORRICK, HERRINGTON & SUTCLIFFE LLP

Dated: June 15, 2005

By: _____
Charles Fowler
Reg. No. 39,675

Orrick, Herrington & Sutcliffe LLP
4 Park Plaza, Suite 1600
Irvine, CA 92614-2558
Tel. 949-567-6700
Fax: 949-567-6710
Customer Number: 34313

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/776,037	Confirmation No.: 1520
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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL DECLARATION OF FACTS IN SUPPORT OF FILING ON BEHALF OF UNAVAILABLE INVENTORS (37 C.F.R. § 1.47(A))

Sir:

The patent that is the subject of the present application for reissue includes eight listed inventors. Of these, six have executed the Joint Declaration submitted herewith in response to the Notice to File Missing Parts of Reissue Application. Two of the inventors, Niall Herity and Sidney Lo, could not be found despite the diligent efforts of the Assignee and its counsel. This Supplemental Declaration is made as to the exact facts that are relied upon to establish the diligent effort made to secure the execution of the Joint Declaration by the unavailable inventors, Niall Herity and Sidney Lo, for the above-identified reissue patent application.

This Declaration is being made by the available person having first-hand knowledge of the facts recited herein.

CERTIFICATE OF MAILING
37 CFR §1.8

I hereby certify, pursuant to 37 CFR §1.8, that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) would be mailed or transmitted on or before the date indicated with the United States Postal Service with sufficient postage as first class mail on the date shown below in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Dated: June 15, 2005

Valerie Cloyd

Valerie M. Cloyd

IDENTIFICATION OF PERSON MAKING THIS DECLARATION OF FACTS

Name of Declarant: Charles C. Fowler

Address of Declarant: Orrick, Herrington & Sutcliffe LLP, 4 Park Plaza, Suite 1600, Irvine, California 92614-2558

LAST KNOWN ADDRESS OF THE OMITTED/UNAVAILABLE INVENTOR

Name of omitted/unavailable inventor: Niall Herity

Last known address of omitted/unavailable inventor: 24 Baronscourt Heights, Carryduff BT8 8RS, Northern Ireland

Name of omitted/unavailable inventor: Sidney Lo

Last known address of omitted/unavailable inventor: 2/29 Marshall Street, Surry Hills 2010, Sydney, Australia

DETAILS OF DILIGENT EFFORT TO SECURE THE SIGNATURE OF THE UNAVAILABLE INVENTORS

1. Ms. Kari Guy, an employee of Stanford University, the assignee of the present application, confirmed in a letter dated February 17, 2004, that Dr. Niall Herity and Dr. Sidney Lo were not associated with Stanford University. In the letter, Ms. Guy provided the last known addresses listed above, telephone numbers for both inventors, and an e-mail addresses for Dr. Herity. A copy of Ms. Guy's letter is attached as Exhibit A.

2. Between May 18, 2004 and June 15, 2004, I made attempts to contact Dr. Herity by telephone and by e-mail, using the information provided by Ms. Guy. A copy of an e-mail sent to Dr. Herity's last known e-mail address is attached as Exhibit B. I was not able to reach Dr. Herity, nor did Dr. Herity respond to my e-mail. During the same time period, I made attempts to contact Dr. Lo by telephone, but was not able to reach Dr. Lo.

3. In mid-June of 2004, Ms. Guy confirmed to me by e-mail that the mailing addresses specified above are Dr. Herity's and Dr. Lo's last addresses known to Stanford University.

4. Letters were sent to each of Dr. Herity and Dr. Lo at their last known addresses on June 15, 2004. The letters enclosed copies of the reissue patent application, the preliminary amendment, the statement of status / support for changes to claims, and the draft of the joint declaration. The letters requested that Dr. Herity and Dr. Lo contact me by no later than July 2, 2004. A copy of the letter (including attachments) sent to Dr. Herity is attached as Exhibit C. A copy of the letter (including attachments) sent to Dr. Lo is attached as Exhibit D.

5. I have not been contacted by either of Dr. Herity or Dr. Lo in response to the letters referred to in paragraph 4.

6. On June 15, 2005, I performed an online search of the Australian Telstra White Pages database (http:www.whitepages.com.au/wp/resSearch.jhtml) to attempt to find the current address for Dr. Lo. A printout of the search results is attached as Exhibit E. Of the 58 entries returned from the search for "S Lo", none was consistent with the address and telephone number last known for Dr. Lo.

7. On June 15, 2005, I performed an online search of the British Telecom database (http://www2.bt.com/edq_resnamesearch?namespace=coexistence) to attempt to find the current address for Dr. Herity. A printout of the search results is attached as Exhibit F. No result of "N Herity" was returned from the search of surname "Herity" and town "Carryduff."

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and

further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such statements may jeopardize the validity of the application or any patent issued thereon.

Dated: June 15, 2005

By: _____
Charles Fowler

February 17, 2004

James Geriak, Esq.
Orrick, Herrington & Sutcliffe
4 Park Plaza
Irvine, CA 92614

Re: Patent Dkt. 13854.4004

Dear Mr. Geriak,

Enclosed is the original patent document Dkt. 13854.4004 sent to Dr. Paul Yock for signatures. We have collected signatures for all of the Stanford staff. The following parties are not at Stanford, so I was not able to obtain their signatures.

Andy Carter, MD
Northwest HeartCare
9155 S.W. Barnes Road, Suite 204
Portland, OR 97225
503.216.5206

Niall Herity, MD
24 Baronscourt Heights
Carryduff BT8 8RS
Northern Ireland
44.28.90815816
herity@aol.com

Sidney Lo, MD
2/29 Marshall Street
Surry Hills 2010
Sydney, Australia
61.2.9.3606041

Please feel free to call me at the number below if you have any questions.

Regards,

Kari Guy

Kari Guy
Administrative Assistant to Dr. Yock

Fowler, Charles C.

From: Fowler, Charles C.
Sent: Wednesday, June 02, 2004 10:34 AM
To: 'herity@aol.com'
Subject: Stanford University / United States Patent Matter

Dear Dr. Herity:

I am Chuck Fowler, a patent attorney with the Orrick, Herrington & Sutcliffe law firm. I am based in Irvine, California, USA. We represent Venomatrix, which is the exclusive licensee from Stanford University of United States Patent No. 6,346,098 ("the '098 patent"), for which you are one of eight listed inventors. We also have a power of attorney from Stanford relating to prosecution of the '098 patent. I was given your contact information by Dr. Paul Yock's office at Stanford. I am contacting you to arrange to have you execute a document relating to the '098 patent.

The '098 patent relates to "Methods and Kits for Locally Administering an Active Agent to a Host." Stanford and VenoMatrix have decided to pursue a reissue of the patent, which is needed to correct several of the claims in the patent and to add several others. In order to do so, we will need to have all of the inventors execute a declaration setting forth the basis for the shortcomings in the patent claims. Dr. Yock and the other inventors residing in the US have already executed the declaration.

Please send me a return e-mail as soon as possible to let me know that you received this message. Please also let me know the best way to forward the documents to you for your signature. I can send them to you electronically (.PDF format) or by mail. If it is to be by mail, please let me have the best address to reach you. The one that I have is the following:

Dr. Niall Herity
24 Baronscourt Heights
Carryduff BT8 8RS
Northern Ireland

Finally, please let me know if you have any questions about the reissue process or it contents.

Thank you for your attention to this matter, and please contact me if you have any questions.

Best regards,
Chuck Fowler

Charles C. Fowler
Orrick Herrington & Sutcliffe LLP
4 Park Plaza, Suite 1600
Irvine, California 92614

(949) 567-6700 Telephone
(949) 567-6710 Facsimile
ccfowler@orrick.com Email
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IRVINE, CA 92614-2558
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fax 949-567-6710
WWW.ORRICK.COM

June 15, 2004

Charles C. Fowler
(949) 567-6700
cfowler@orrick.com

Niall Herity, MD
24 Baronscourt Heights
Carryduff BT8 8RS
Northern Ireland

Re: U.S. Reissue Patent Application No. 10/776,037
For: METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST
Our Docket: 13854.4004

Dear Dr. Herity:

We represent Venomatrix, the exclusive licensee from Stanford University ("Stanford") of United States Patent No. 6,346,098 ("the '098 patent"), on which you are a named inventor. We also have power of attorney to represent Stanford for the purpose of prosecuting the '098 patent. Stanford and Venomatrix have determined that the claims of the '098 patent are inadequate to cover the full extent of the inventions described in the patent. In order to correct these errors, we have filed, on behalf of Stanford, an application for reissue of the '098 patent.

Which brings us to the purpose for this letter. In order to prosecute the reissue application, we must submit to the United States Patent and Trademark Office a declaration from all of the '098 patent inventors setting forth the errors that give rise to the reissue application. In this case, this amounts to describing the manner in which the claims are inadequate to cover the full extent of the inventions described in the patent. A copy of this "Joint Declaration" is enclosed. Please review this document and, if it is accurate, sign and date it where indicated and return it to us in the enclosed envelope.

In order to answer some of the questions that you might have, we have enclosed copies of the reissue application papers, including the following:

1. A "Power of Attorney" executed on behalf of Stanford University granting Orrick, Herrington & Sutcliffe LLP the authority to prosecute the reissue application;

2. A copy of the '098 patent;

3. A "Preliminary Amendment" that includes all of the revisions and additions to the '098 patent claims being sought in the reissue application;

4. A "Statement of Status / Support for Changes to Claims" for identifying the portions of the '098 patent specification that support the proposed amendments; and

5. Two copies (one for your records, one to execute and return to us) of a "Joint Declaration" of all of the '098 patent inventors.

Please review the application papers and contact me with any questions. I can be reached by telephone at (949) 852-7770 (direct dial), or by e-mail at ccfowler@orrick.com. If you do not have any questions, please execute the "Joint Declaration" where indicated in the space provided on page 11, and return it to me in the enclosed self-addressed, stamped envelope. **In either event, please return the executed declaration by no later than July 2, 2004.**

Please contact me if you have any questions.

Very truly yours,

ORRICK, HERRINGTON & SUTCLIFFE LLP

Charles C. Fowler

CCF/vmc
Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	Not yet assigned.	Confirmation No.:
		Reissue of US Patent No. 6,346,098 B1	
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

POWER OF ATTORNEY AND
CERTIFICATION UNDER 37 C.F.R. 3.73(b)

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The assignee of record of the entire interest of the above-identified application hereby appoints the registered practitioners at Customer No. 34313:

Orrick, Herrington & Sutcliffe, LLP
4 Park Plaza, Suite 1600
Irvine, California 92614-2558
Tel.: (949) 567-6700

as its attorneys/agents with full power of substitution and revocation to prosecute this application, to transact all business in the Patent and Trademark Office, in connection therewith, and to receive any Letters Patent.

Please send all correspondence to the attention of James W. Geriak, at the above Customer Number and address, and direct all telephone calls to **(949) 567-6700.**

Applicant	:	Paul G. Yock, et al.
Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1
Examiner	:	Not yet assigned.
Docket No.	:	13854.4004

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a non-profit organization organized and existing under and by virtue of the laws of the State of California, certifies that it is the assignee of the entire right, title, and interest in the application(s) identified above by virtue of an assignment from the inventor(s) of the original patent application to which the application identified above corresponds, including all reissues therefrom. The assignment of which was recorded in the Patent and Trademark Office on August 7, 2000 at Reel 011118 and Frame 0455.

The undersigned (whose title is supplied below) is empowered to act on behalf of the assignee.

I hereby declare that all statements made herein are of my own knowledge and are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing thereon.

Dated: February 5, 2004

By: Katharine Ku
Name: Katharine Ku
Title: Director, Office of Technology Licensing

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	Not yet assigned.	Confirmation No.:
		Reissue of US Patent No. 6,346,098 B1	
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner for Patents
Mail Stop Reissue
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Dear Sir/Madam:

In connection with the Application for Reissue filed herewith, and prior to examination thereof, please amend the above-identified application as follows:

CERTIFICATE OF MAILING
37 CFR §1.10

Date: February 9, 2004
Express Mailing Label No.: EV228108745US

I hereby certify that on the dated listed above, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as "Express Mail Post Office to Addressee," with sufficient postage in an envelope addressed to: Mail Stop Patent Application, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Valerie Cloyd

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Original) A method of locally administrating an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.

2. (Original) The method according to claim 1, wherein said vessel is a vein.

3. (Original) The method according to claim 1, wherein said retroinfusing comprises providing stress to said vascular vessel at a site at least proximal to said interstitial space.

4. (Original) The method according to claim 1, wherein said method further comprises using depot means.

5. (Original) The method according to claim 1, wherein said method further comprises administration of energy to said vessel.

6. (Original) The method according to claim 1, wherein said interstitial space is myocardial interstitial space.

7. (Original) The method according to claim 3, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vessel.

8. (Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said [vessel] vein and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.

9. (Original) The method according to claim 8, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vein.

10. (Original) The method according to claim 8, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

11. (Amended) The method according to claim 8, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.

12. (Original) The method according to claim 8, wherein said interstitial space is myocardial interstitial space.

13. (Original) The method according to claim 9, wherein said pressure is sufficient to at least distend said vein.

14. (Original) The method according to claim 9, wherein said pressure is sufficient to disrupt said vein.

15. (Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient to produce a disruption [on] in said vein such that said agent enters an interstitial space proximal to the vein through said disruption;

whereby said agent is locally administered to said host.

16. (Original) The method according to claim 15, wherein said pressure is sufficient to at least distend said vein.

17. (Original) The method according to claim 16, wherein said pressure is sufficient to disrupt said vein.

18. (Original) The method according to claim 16, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

19. (Amended) The method according to claim 16, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.

20. The method of claim 1 wherein said agent comprises cells.

21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.

23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.

24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.

25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

29. The method of claim 3 wherein said stress is chemical stress.

30. The method of claim 1 wherein said vessel is an artery.

31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.

34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

35. The method of claim 34 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.

37. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and infusing said agent into an interstitial space of said

host through said disruption and locally administering said agent to said host through said disruption.

38. The method according to claim 37, wherein said vessel is a vein.

39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.

40. The method according to claim 37, wherein said method further comprises using depot means.

41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.

42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.

43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

44. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host under conditions sufficient to produce a disruption in said vein and infusing said agent into an interstitial space of said host through said disruption so that said agent is locally administered to said host.

45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.

46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.

48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.

49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.

50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.

51. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption;

whereby said agent is locally administered to said host.

52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.

53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.

54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.

56. A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

57. The method according to claim 56, wherein said pressure is sufficient to at least distend said vessel.

58. The method according to claim 56, wherein said pressure is sufficient to disrupt said vessel.

59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.

61. The method of claim 56 wherein said vessel is an artery.

62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.

65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

67. A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

69. The method according to claim 67, wherein said pressure is sufficient to disrupt said vessel.

70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.

72. The method of claim 67 wherein said vessel is an artery.

73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.

76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

78. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host.

79. The method according to claim 78, wherein said vessel is a vein.

80. The method according to claim 78, wherein said pressure is sufficient to at least distend said vessel.

81. The method according to claim 78, wherein said pressure is sufficient to disrupt said vessel.

82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.

84. The method of claim 78 wherein said vessel is an artery.

85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.

88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

90. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

91. The method according to claim 90, wherein said vessel is a vein.

92. The method according to claim 90, wherein said pressure is sufficient to disrupt said vessel.

93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.

95. The method of claim 90 wherein said vessel is an artery.

96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.

99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

Remarks

This preliminary amendment concerns the reissue application submitted herewith. By this amendment, original claims 8, 11, 15, and 19 are amended, and new claims 20 through 100 are added.

The claim amendments are minor. The amendment to claim 8 changes the word "vessel" to "vein", in order to reconcile the recitation with its antecedent. The amendment to claim 11 corrects the misspelling of "inflammation," and also changes "vessel" to "vein" to reconcile with the recitation in the independent claim. The amendment to claim 15 changes the word "on" in the phrase "on said vein" to, more appropriately, "in". Finally, the amendment to claim 19, like the amendment to claim 11, corrects the misspelling of "inflammation" and changes "vessel" to "vein" to reconcile with the recitation in the independent claim.

The new claims, 20 through 100, are intended to correct the errors discussed in the Joint Declaration of the Inventors submitted herewith. Of these claims, claims 20 through 36 all depend (either directly or indirectly) from original claim 1. Claims 37 through 55 generally track original claims 1 through 19, but include recitation of retroinfusing "a fluid" rather than retroinfusing "said agent," thereby broadening those claims relative to the original patent claims. New independent claim 56 generally tracks original claim 7, but clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New independent claim 67 generally tracks original claim 13, but similarly clarifies that the distention "facilitates the transport of said agent through the wall of said

vessel." New independent claim 78 generally tracks original claim 7, but (like new independent claim 56) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 78 (and its dependent claims, 79-89) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims. Finally, new independent claim 90 generally tracks original claim 13, but (like new independent claim 67) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 90 (and its dependent claims, 91-100) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims.

Specification support for all of the amendments and new claims is listed in the Statement of Status / Support for Changes to Claims submitted herewith. No new matter is added by this amendment.

CONCLUSION

In view of the foregoing, it is submitted that the claims presented in this reissue application define patentable subject matter to which Applicant is entitled. Accordingly, consideration and allowance of the reissue application is requested.

Respectfully submitted,

Orrick, Herrington & Sutcliffe LLP

Dated: Feb. 3, 2004

By _____

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1	Confirmation No.:
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner for Patents
Mail Stop Reissue
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT OF STATUS / SUPPORT FOR CHANGES TO CLAIMS UNDER 37 C.F.R. § 1.173(c)

Dear Sir/Madam:

In connection with the Application for Reissue and Preliminary Amendment filed herewith, the following is a statement of status of all patent claims and of all added claims as of the date of the Preliminary Amendment, and an explanation of the support in the disclosure of the patent for the changes made to the claims.

CERTIFICATE OF MAILING
37 CFR §1.10

Date: February 9, 2004
Express Mailing Label No.: EV228108745US

I hereby certify that on the dated listed above, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as "Express Mail Post Office to Addressee," with sufficient postage in an envelope addressed to: Mail Stop Patent Application, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Valerie Cloyd

Status of Claims

As of the date of the Preliminary Amendment submitted herewith, the status of the claims is as follows:

Claims 1 through 100 are pending.

Support for Changes Made to Claims

Of the pending claims, the following changes have been made by the Preliminary Amendment submitted herewith:

Claims 8, 11, 15, and 19 have been amended.

Claims 20 through 100 have been added.

The support in the disclosure of the patent for each of the above changes is set forth in the table below.

Amended / New Claim	Support in Patent Disclosure
8. (Amended) A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said [vessel] vein and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Amendment is to correct error in claim because there is no antecedent for "said vessel" in claim. The proper antecedent is "vein" rather than "vessel." Support for "vein" appears at col. 3, line 18, and col. 2, line 22.
11. (Amended) The method according to claim 8, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.	Same as Claim 8, plus correction of spelling of "inflammation." Col. 4, lines 62-64.

Amended / New Claim	Support in Patent Disclosure
15. (Amended) A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient to produce a disruption [on] <u>in</u> said vein such that said agent enters an interstitial space proximal to the vein through said disruption; whereby said agent is locally administered to said host.	Amendment corrects grammatical error.
19. (Amended) The method according to claim 16, wherein said method further comprises producing [inflamation] <u>inflammation</u> in said [vascular vessel] <u>vein</u>.	Same as Claim 11.
20. The method of claim 1 wherein said agent comprises cells.	Col. 8, line 37.
21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.	Col. 7, line 55.
23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.	Col. 7, line 58.
24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.	Col. 8, lines 28-31.

Amended / New Claim	Support in Patent Disclosure
25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.	Col. 5, line 56.
26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.	Col. 5, line 56.
27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.	Col. 5, line 58.
28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.	Col. 6, lines 13-47.
29. The method of claim 3 wherein said stress is chemical stress.	Col. 6, lines 48-51.
30. The method of claim 1 wherein said vessel is an artery.	Col. 3, line 18.
31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

Amended / New Claim	Support in Patent Disclosure
33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
35. The method of claim 35 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.
36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
37. A method of locally administrating an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and infusing said agent into an interstitial space of said host through said disruption and locally administering said agent to said host through said disruption.	Col. 4, line 54.
38. The method according to claim 37, wherein said vessel is a vein.	Col. 2, line 22.

Amended / New Claim	Support in Patent Disclosure
39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.	Col. 2, lines 21-24
40. The method according to claim 37, wherein said method further comprises using depot means.	Col. 9, lines 1 and 2.
41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.	Col. 6, lines 1-8.
42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
44. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vein of said host under conditions sufficient to produce a disruption in said vein and infusing said agent into an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Col. 4, lines 52-55.

Amended / New Claim	Support in Patent Disclosure
45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.	Col. 1, line 66 – Col. 2, line 2.
46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.	Col. 4, lines 62-64.
48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.	Col. 5, lines 19-23.
50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.	Col. 5, lines 35-36.

Amended / New Claim	Support in Patent Disclosure
51. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption; whereby said agent is locally administered to said host.	Col. 4, line 54.
52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.	Col. 5, lines 19-23.
53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.	Col. 5, lines 35-36.
54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.	Col. 4, lines 62-64.

Amended / New Claim	Support in Patent Disclosure
56. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 4, line 54.
57. The method according to claim 56, wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
58. The method according to claim 56, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
61. The method of claim 56 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
67. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 5, lines 19-23.
68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
69. The method according to claim 67, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
72. The method of claim 67 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
78. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host.	Col. 4, line 54; Col. 1, line 66 – Col. 2, line 2.
79. The method according to claim 78, wherein said vessel is a vein.	Col. 2, line 22.
80. The method according to claim 78, wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
81. The method according to claim 78, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
84. The method of claim 78 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
90. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 5, lines 19-23; Col. 1, line 66 – Col. 2, line 2.
91. The method according to claim 90, wherein said vessel is a vein.	Col. 2, line 22.
92. The method according to claim 90, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
95. The method of claim 90 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

Applicant	:	Paul G. Yock, et al.
Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1
Examiner	:	Not yet assigned.
Docket No.	:	13854.4004

Amended / New Claim	Support in Patent Disclosure
100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Respectfully submitted,

Orrick, Herrington & Sutcliffe LLP

Dated: Feb. 3, 2004

By _____
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Patent
Dkt. 13854.4004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Application of: Paul G. Yock, et al. Serial No.: Not yet Assigned, Reissue of U.S. Patent No. 6,346,098 B1 Filed: Herewith For: METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	Group Art Unit: Not Yet Assigned Examiner: Not yet assigned Reissue Application of U.S. Patent No. 6,346,098 B1

JOINT DECLARATION OF PAUL G. YOCK, ALI H. HASSAN, ALAN CHING YEUN YEUNG, ANDREW CARTER, MEHRDAD REZAEE, NIALL HERITY, SIDNEY LO, AND PETER J. FITZGERALD UNDER 37 C.F.R. 1.175

We, Paul G. Yock, Ali H. Hassan, Alan Ching Yeun Yeung, Andrew Carter, Mehrdad Rezaee, Niall Herity, Sidney Lo, and Peter J. Fitzgerald jointly declare:

1. Each of our residence address, mailing address, and countries of citizenship are stated below next to our names.

CERTIFICATE OF MAILING
(37 C.F.R. §1.8

I hereby certify, pursuant to 37 CFR §1.8, that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) would be mailed or transmitted on or before the date indicated with the United States Postal Service with sufficient postage as first class mail on the date shown below in an envelope addressed to Mail Stop Reissue, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date of Deposit

Signature of Person Mailing Paper

2. We believe that we are the original, first, and joint inventors of the subject matter described and claimed in United States Patent No. 6,346,098 B1 (hereinafter "the '098 Patent"), granted on February 12, 2002, and for which a reissue patent is sought on the invention entitled "Methods and Kits for Locally Administering an Active Agent to an Interstitial Space of a Host," the specification of which is submitted concurrently with this Declaration.

3. We do not know and do not believe that the invention was ever known in the United States of America before our invention thereof.

4. We believe that the '098 Patent may be partly inoperative or invalid by reason of the patentee claiming more or less than patentee had the right to claim in the patent.

5. This application is, in part, a broadening reissue application, and that an explanation of the nature of the broadening is set forth below.

6. At least one error in the original claims of the '098 Patent upon which reissue is based is described below.

7. The original claims of the '098 Patent each recited a method of locally administering an active agent to a host, but that several embodiments of the methods described in the '098 Patent, for which we are rightfully entitled to coverage by the claims of the '098 Patent, were not recited in the original claims, including the following (which are recited in new dependent claims 20-36):

a. The method recited in original claim 1 wherein said agent comprises cells.

b. The method recited in original claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

c. The method recited in original claim 1, wherein said agent comprises therapeutic nucleic acids.

d. The method recited in original claim 1, wherein the agent comprises therapeutic nucleic acids, and wherein the therapeutic nucleic acids comprise at least one gene.

e. The method recited in original claim 1, wherein said agent comprises a dye or an imaging agent.

f. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

g. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

h. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

i. The method recited in original claim 5, wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

j. The method recited in original claim 3, wherein said stress is chemical stress.

k. The method recited in original claim 1, wherein said vessel is an artery.

l. The method recited in original claim 2, wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

m. The method recited in original claim 1, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

n. The method recited in original claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent, and wherein at least one upstream branch of said vessel is occluded.

o. The method recited in original claim 2, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

p. The method recited in original claim 2, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site

of administration of said agent, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

q. The method recited in original claim 1, wherein said pressure is sufficient to at least distend said vessel.

8. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 7 and 7.a. through 7.q. are corrected by the inclusion of new claims 20 through 36, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, one of embodiments listed in paragraphs 7.a. through 7.q. that was not recited in the original claims of the '098 Patent.

9. The original claims of the '098 Patent, including independent claims 1, 8, and 13, each recite a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing said agent into a vascular vessel (claim 1) or vein (claims 8 and 13), whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing a fluid into a vascular vessel or vein followed by retroinfusing the agent, and, accordingly, that the claims thereof are insufficient because they are unnecessarily limiting.

10. The insufficiency of the original claims of the '098 Patent set forth in the paragraph 9 is corrected by the inclusion of new claims 37 through 55, each of which recites a

method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent, thereby presenting claims that are broader in this respect than the original claims of the '098 Patent.

11. Original claim 7 of the '098 Patent recites a method of locally administering an active agent to a host comprising, *inter alia*, administering an agent at a pressure sufficient to produce at least a mechanical stress on said vessel, whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host, and, accordingly, that the claims thereof are insufficient because they do not recite the foregoing methodology.

12. The insufficiency of the original claims of the '098 Patent set forth in the paragraph 11 is corrected by the inclusion of new claims 56 through 66, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

13. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 9 and 11 are further corrected by the inclusion of new claims 78 through 89, each of which

recites a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent – thereby presenting claims that are broader in this respect than the original claims of the '098 Patent – and each of which further recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

14. Original claim 13 of the '098 Patent recites a method of locally administering an active agent to a host comprising, *inter alia*, administering an agent at a pressure sufficient to at least distend a vein of the host, whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension facilitates the transport of the agent through the wall of the vein so that the agent is locally administered to the host, and, accordingly, that the claims thereof are insufficient because they do not recite the foregoing methodology.

15. The insufficiency of the original claims of the '098 Patent set forth in paragraph 14 is corrected by the inclusion of new claims 67 through 77, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension

facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

16. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 9 and 14 are further corrected by the inclusion of new claims 90 through 100, each of which recites a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent – thereby presenting claims that are broader in this respect than the original claims of the '098 Patent – and each of which further recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

17. The insufficiencies in the original claims of the '098 Patent identified in paragraphs 7, 7.a.-7.q., 9, 11, and 14 arose, occurred or resulted from the fact that we and our attorneys failed to communicate adequately concerning the preparation of claims and prosecution of the application that issued as the '098 patent, and that our attorneys failed to appreciate the full scope of the invention and that the original claims would possibly preclude coverage of embodiments of the invention that are disclosed and supported by the patent specification, which embodiments are within a scope of coverage to which we are rightfully entitled.

18. Original claim 8 included recitation of "retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said vessel," whereas the term "vessel" should have been "vein" in order to properly reflect its antecedent.

19. Original claim 11 included recitation of a method that produces "inflamation" [sic] in said "vascular vessel," whereas it should have recited "inflammation in said vein".

20. Original claim 15 included recitation of pressure sufficient to produce a disruption "on" said vein, whereas it should have recited pressure sufficient to produce a disruption "in" said vein.

21. Original claim 19 included recitation of a method that produces "inflamation" [sic] in said "vascular vessel," whereas it should have recited "inflammation in said vein".

22. Each of claims 8, 11, 15, and 19 are amended in the Preliminary Amendment to correct the formal errors set forth in the preceding four paragraphs.

23. All of the aforementioned errors in the original patent that are being corrected in the reissue application up to the time of filing of this declaration arose without any deceptive intention on the part of any of us.

24. Each of us has reviewed and understands the contents of the above-identified application for Patent Reissue and the Preliminary Amendment filed herewith.

25. Each of us acknowledges the duty to disclose information which is material to the examination of this Application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a).

26. All statements made herein of our own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like may jeopardize the validity of this application for reissue or any patent issuing thereon.

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June 15, 2004

Charles C. Fowler
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Sidney Lo, MD
2/29 Marshall Street
Surry Hills 2010
Sydney
Australia

Re: U.S. Reissue Patent Application No. 10/776,037
For: METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST
Our Docket: 13854.4004

Dear Dr. Lo:

We represent Venomatrix, the exclusive licensee from Stanford University ("Stanford") of United States Patent No. 6,346,098 ("the '098 patent"), on which you are a named inventor. We also have power of attorney to represent Stanford for the purpose of prosecuting the '098 patent. Stanford and Venomatrix have determined that the claims of the '098 patent are inadequate to cover the full extent of the inventions described in the patent. In order to correct these errors, we have filed, on behalf of Stanford, an application for reissue of the '098 patent.

Which brings us to the purpose for this letter. In order to prosecute the reissue application, we must submit to the United States Patent and Trademark Office a declaration from all of the '098 patent inventors setting forth the errors that give rise to the reissue application. In this case, this amounts to describing the manner in which the claims are inadequate to cover the full extent of the inventions described in the patent. A copy of this "Joint Declaration" is enclosed. Please review this document and, if it is accurate, sign and date it where indicated and return it to us in the enclosed envelope.

In order to answer some of the questions that you might have, we have enclosed copies of the reissue application papers, including the following:

1. A "Power of Attorney" executed on behalf of Stanford University granting Orrick, Herrington & Sutcliffe LLP the authority to prosecute the reissue application;

2. A copy of the '098 patent;

3. A "Preliminary Amendment" that includes all of the revisions and additions to the '098 patent claims being sought in the reissue application;

4. A "Statement of Status / Support for Changes to Claims" for identifying the portions of the '098 patent specification that support the proposed amendments; and

5. Two copies (one for your records, one to execute and return to us) of a "Joint Declaration" of all of the '098 patent inventors.

Please review the application papers and contact me with any questions. I can be reached by telephone at (949) 852-7770 (direct dial), or by e-mail at ccfowler@orrick.com. If you do not have any questions, please execute the "Joint Declaration" where indicated in the space provided on page 11, and return it to me in the enclosed self-addressed, stamped envelope. **In either event, please return the executed declaration by no later than July 2, 2004.**

Please contact me if you have any questions.

Very truly yours,

ORRICK, HERRINGTON & SUTCLIFFE LLP

Charles C. Fowler

CCF/vmc
Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

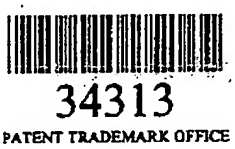
Appl. No.	:	Not yet assigned.	Confirmation No.:
		Reissue of US Patent No. 6,346,098 B1	
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

POWER OF ATTORNEY AND
CERTIFICATION UNDER 37 C.F.R. 3.73(b)

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The assignee of record of the entire interest of the above-identified application hereby appoints the registered practitioners at Customer No. 34313:



Orrick, Herrington & Sutcliffe, LLP
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as its attorneys/agents with full power of substitution and revocation to prosecute this application, to transact all business in the Patent and Trademark Office, in connection therewith, and to receive any Letters Patent.

Please send all correspondence to the attention of James W. Geriak, at the above Customer Number and address, and direct all telephone calls to **(949) 567-6700.**

Applicant	:	Paul G. Yock, et al.
Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1
Examiner	:	Not yet assigned.
Docket No.	:	13854.4004

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a non-profit organization organized and existing under and by virtue of the laws of the State of California, certifies that it is the assignee of the entire right, title, and interest in the application(s) identified above by virtue of an assignment from the inventor(s) of the original patent application to which the application identified above corresponds, including all reissues therefrom. The assignment of which was recorded in the Patent and Trademark Office on August 7, 2000 at Reel 011118 and Frame 0455.

The undersigned (whose title is supplied below) is empowered to act on behalf of the assignee.

I hereby declare that all statements made herein are of my own knowledge and are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing thereon.

Dated: February 5, 2004

By: Katharine Ku

Name: Katharine Ku
Title: Director, Office of Technology Licensing

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	Not yet assigned.	Confirmation No.:
		Reissue of US Patent No. 6,346,098 B1	
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner for Patents
Mail Stop Reissue
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Dear Sir/Madam:

In connection with the Application for Reissue filed herewith, and prior to examination thereof, please amend the above-identified application as follows:

CERTIFICATE OF MAILING
37 CFR §1.10

Date: February 9, 2004
Express Mailing Label No.: EV228108745US

I hereby certify that on the dated listed above, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as "Express Mail Post Office to Addressee," with sufficient postage in an envelope addressed to: Mail Stop Patent Application, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Valerie Cloyd

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Original) A method of locally administrating an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.

2. (Original) The method according to claim 1, wherein said vessel is a vein.

3. (Original) The method according to claim 1, wherein said retroinfusing comprises providing stress to said vascular vessel at a site at least proximal to said interstitial space.

4. (Original) The method according to claim 1, wherein said method further comprises using depot means.

5. (Original) The method according to claim 1, wherein said method further comprises administration of energy to said vessel.

6. (Original) The method according to claim 1, wherein said interstitial space is myocardial interstitial space.

7. (Original) The method according to claim 3, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vessel.

8. (Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said [vessel] vein and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.

9. (Original) The method according to claim 8, wherein said retroinfusing comprises administering said agent at a pressure sufficient to produce at least a mechanical stress on said vein.

10. (Original) The method according to claim 8, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

11. (Amended) The method according to claim 8, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.

12. (Original) The method according to claim 8, wherein said interstitial space is myocardial interstitial space.

13. (Original) The method according to claim 9, wherein said pressure is sufficient to at least distend said vein.

14. (Original) The method according to claim 9, wherein said pressure is sufficient to disrupt said vein.

15. (Amended) A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient to produce a disruption [on] in said vein such that said agent enters an interstitial space proximal to the vein through said disruption;

whereby said agent is locally administered to said host.

16. (Original) The method according to claim 15, wherein said pressure is sufficient to at least distend said vein.

17. (Original) The method according to claim 16, wherein said pressure is sufficient to disrupt said vein.

18. (Original) The method according to claim 16, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

19. (Amended) The method according to claim 16, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.

20. The method of claim 1 wherein said agent comprises cells.

21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.

23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.

24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.

25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

29. The method of claim 3 wherein said stress is chemical stress.

30. The method of claim 1 wherein said vessel is an artery.

31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.

34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

35. The method of claim 34 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.

37. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and infusing said agent into an interstitial space of said

host through said disruption and locally administering said agent to said host through said disruption.

38. The method according to claim 37, wherein said vessel is a vein.

39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.

40. The method according to claim 37, wherein said method further comprises using depot means.

41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.

42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.

43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

44. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host under conditions sufficient to produce a disruption in said vein and infusing said agent into an interstitial space of said host through said disruption so that said agent is locally administered to said host.

45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.

46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.

48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.

49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.

50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.

51. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption;

whereby said agent is locally administered to said host.

52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.

53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.

54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.

56. A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

57. The method according to claim 56, wherein said pressure is sufficient to at least distend said vessel.

58. The method according to claim 56, wherein said pressure is sufficient to disrupt said vessel.

59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.

61. The method of claim 56 wherein said vessel is an artery.

62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.

65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

67. A method of locally administering an active agent to a host, said method comprising:

retroinfusing said agent into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.

69. The method according to claim 67, wherein said pressure is sufficient to disrupt said vessel.

70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.

72. The method of claim 67 wherein said vessel is an artery.

73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.

76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

78. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host.

79. The method according to claim 78, wherein said vessel is a vein.

80. The method according to claim 78, wherein said pressure is sufficient to at least distend said vessel.

81. The method according to claim 78, wherein said pressure is sufficient to disrupt said vessel.

82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.

84. The method of claim 78 wherein said vessel is an artery.

85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.

88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

90. A method of locally administering an active agent to a host, said method comprising:

retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.

91. The method according to claim 90, wherein said vessel is a vein.

92. The method according to claim 90, wherein said pressure is sufficient to disrupt said vessel.

93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.

95. The method of claim 90 wherein said vessel is an artery.

96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.

99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

Remarks

This preliminary amendment concerns the reissue application submitted herewith. By this amendment, original claims 8, 11, 15, and 19 are amended, and new claims 20 through 100 are added.

The claim amendments are minor. The amendment to claim 8 changes the word "vessel" to "vein", in order to reconcile the recitation with its antecedent. The amendment to claim 11 corrects the misspelling of "inflammation," and also changes "vessel" to "vein" to reconcile with the recitation in the independent claim. The amendment to claim 15 changes the word "on" in the phrase "on said vein" to, more appropriately, "in". Finally, the amendment to claim 19, like the amendment to claim 11, corrects the misspelling of "inflammation" and changes "vessel" to "vein" to reconcile with the recitation in the independent claim.

The new claims, 20 through 100, are intended to correct the errors discussed in the Joint Declaration of the Inventors submitted herewith. Of these claims, claims 20 through 36 all depend (either directly or indirectly) from original claim 1. Claims 37 through 55 generally track original claims 1 through 19, but include recitation of retroinfusing "a fluid" rather than retroinfusing "said agent," thereby broadening those claims relative to the original patent claims. New independent claim 56 generally tracks original claim 7, but clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New independent claim 67 generally tracks original claim 13, but similarly clarifies that the distention "facilitates the transport of said agent through the wall of said

vessel." New independent claim 78 generally tracks original claim 7, but (like new independent claim 56) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 78 (and its dependent claims, 79-89) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims. Finally, new independent claim 90 generally tracks original claim 13, but (like new independent claim 67) clarifies that the mechanical stress "facilitates the transport of said agent through the wall of said vessel." New claim 90 (and its dependent claims, 91-100) also includes recitation of retroinfusing "a fluid" rather than retroinfusing "said agent", thereby broadening those claims relative to the original claims.

Specification support for all of the amendments and new claims is listed in the Statement of Status / Support for Changes to Claims submitted herewith. No new matter is added by this amendment.

CONCLUSION

In view of the foregoing, it is submitted that the claims presented in this reissue application define patentable subject matter to which Applicant is entitled. Accordingly, consideration and allowance of the reissue application is requested.

Respectfully submitted,

Orrick, Herrington & Sutcliffe LLP

Dated: Feb. 3, 2004

By _____
James W. Geriak
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	Not yet assigned. Reissue of US Patent No. 6,346,098 B1	Confirmation No.:
Applicant	:	Paul G. Yock, et al.	
Filing Date	:	Herewith	
Title	:	METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	
Group Art Unit	:	Not yet assigned.	
Examiner	:	Not yet assigned	
Docket No.	:	13854.4004	
Customer No.	:	34313	

Commissioner for Patents
Mail Stop Reissue
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT OF STATUS / SUPPORT FOR CHANGES TO CLAIMS UNDER 37 C.F.R. § 1.173(c)

Dear Sir/Madam:

In connection with the Application for Reissue and Preliminary Amendment filed herewith, the following is a statement of status of all patent claims and of all added claims as of the date of the Preliminary Amendment, and an explanation of the support in the disclosure of the patent for the changes made to the claims.

CERTIFICATE OF MAILING
37 CFR §1.10

Date: February 9, 2004
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I hereby certify that on the dated listed above, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as "Express Mail Post Office to Addressee," with sufficient postage in an envelope addressed to: Mail Stop Patent Application, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Valerie Cloyd

Status of Claims

As of the date of the Preliminary Amendment submitted herewith, the status of the claims is as follows:

Claims 1 through 100 are pending.

Support for Changes Made to Claims

Of the pending claims, the following changes have been made by the Preliminary Amendment submitted herewith:

Claims 8, 11, 15, and 19 have been amended.

Claims 20 through 100 have been added.

The support in the disclosure of the patent for each of the above changes is set forth in the table below.

Amended / New Claim	Support in Patent Disclosure
8. (Amended) A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said [vessel] vein and for said agent to enter an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Amendment is to correct error in claim because there is no antecedent for "said vessel" in claim. The proper antecedent is "vein" rather than "vessel." Support for "vein" appears at col. 3, line 18, and col. 2, line 22.
11. (Amended) The method according to claim 8, wherein said method further comprises producing [inflamation] inflammation in said [vascular vessel] vein.	Same as Claim 8, plus correction of spelling of "inflammation." Col. 4, lines 62-64.

Amended / New Claim	Support in Patent Disclosure
15. (Amended) A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vein of said host with a catheter and at a pressure sufficient to produce a disruption [on] <u>in</u> said vein such that said agent enters an interstitial space proximal to the vein through said disruption; whereby said agent is locally administered to said host.	Amendment corrects grammatical error.
19. (Amended) The method according to claim 16, wherein said method further comprises producing [inflamation] <u>inflammation</u> in said [vascular vessel] <u>vein</u>.	Same as Claim 11.
20. The method of claim 1 wherein said agent comprises cells.	Col. 8, line 37.
21. The method of claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
22. The method of claim 1 wherein said agent comprises therapeutic nucleic acids.	Col. 7, line 55.
23. The method of claim 22 wherein the therapeutic nucleic acids comprise at least one gene.	Col. 7, line 58.
24. The method of claim 1 wherein said agent comprises a dye or an imaging agent.	Col. 8, lines 28-31.

Amended / New Claim	Support in Patent Disclosure
25. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.	Col. 5, line 56.
26. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.	Col. 5, line 56.
27. The method of claim 1 wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.	Col. 5, line 58.
28. The method of claim 5 wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.	Col. 6, lines 13-47.
29. The method of claim 3 wherein said stress is chemical stress.	Col. 6, lines 48-51.
30. The method of claim 1 wherein said vessel is an artery.	Col. 3, line 18.
31. The method of claim 2 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
32. The method of claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

Amended / New Claim	Support in Patent Disclosure
33. The method of claim 32 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
34. The method of claim 2 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
35. The method of claim 35 wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.
36. The method of claim 1 wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
37. A method of locally administrating an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a disruption in said vessel and infusing said agent into an interstitial space of said host through said disruption and locally administering said agent to said host through said disruption.	Col. 4, line 54.
38. The method according to claim 37, wherein said vessel is a vein.	Col. 2, line 22.

Amended / New Claim	Support in Patent Disclosure
39. The method according to claim 37, wherein said retroinfusing comprises providing stress to said vascular vessel at a site proximal to said interstitial space.	Col. 2, lines 21-24
40. The method according to claim 37, wherein said method further comprises using depot means.	Col. 9, lines 1 and 2.
41. The method according to claim 37, wherein said method further comprises administration of energy to said vessel.	Col. 6, lines 1-8.
42. The method according to claim 37, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
43. The method according to claim 39, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
44. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vein of said host under conditions sufficient to produce a disruption in said vein and infusing said agent into an interstitial space of said host through said disruption so that said agent is locally administered to said host.	Col. 4, lines 52-55.

Amended / New Claim	Support in Patent Disclosure
45. The method according to claim 44, wherein said retroinfusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vein.	Col. 1, line 66 – Col. 2, line 2.
46. The method according to claim 44, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
47. The method according to claim 44, wherein said method further comprises producing inflammation in said vein.	Col. 4, lines 62-64.
48. The method according to claim 44, wherein said interstitial space is myocardial interstitial space.	Col. 4, line 34.
49. The method according to claim 45, wherein said pressure is sufficient to at least distend said vein.	Col. 5, lines 19-23.
50. The method according to claim 45, wherein said pressure is sufficient to disrupt said vein.	Col. 5, lines 35-36.

Amended / New Claim	Support in Patent Disclosure
51. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vein of said host with a catheter and at a pressure sufficient to produce a disruption in said vein and infusing said agent into an interstitial space proximal to the vein through said disruption; whereby said agent is locally administered to said host.	Col. 4, line 54.
52. The method according to claim 51, wherein said pressure is sufficient to at least distend said vein.	Col. 5, lines 19-23.
53. The method according to claim 52, wherein said pressure is sufficient to disrupt said vein.	Col. 5, lines 35-36.
54. The method according to claim 52, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
55. The method according to claim 52, wherein said method further comprises producing inflammation in said vein.	Col. 4, lines 62-64.

Amended / New Claim	Support in Patent Disclosure
56. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to produce at least a mechanical stress on said vessel, which stress facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 4, line 54.
57. The method according to claim 56, wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
58. The method according to claim 56, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
59. The method according to claim 56, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
60. The method according to claim 56, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
61. The method of claim 56 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
62. The method of claim 58 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
63. The method of claim 56 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
64. The method of claim 63 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
65. The method of claim 58 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
66. The method of claim 65 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
67. A method of locally administering an active agent to a host, said method comprising: retroinfusing said agent into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 5, lines 19-23.
68. The method according to claim 67, wherein said retrofusing comprises administering said fluid at a pressure sufficient to produce at least a mechanical stress on said vessel.	Col. 1, line 66 – Col. 2, line 2.
69. The method according to claim 67, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
70. The method according to claim 67, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
71. The method according to claim 67, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
72. The method of claim 67 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
73. The method of claim 69 wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
74. The method of claim 67 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
75. The method of claim 74 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
76. The method of claim 69, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
77. The method of claim 76, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
78. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to produce a mechanical stress in said vessel, which stress facilitates the transport of said agent through a wall of said vessel so that said agent is locally administered to said host.	Col. 4, line 54; Col. 1, line 66 – Col. 2, line 2.
79. The method according to claim 78, wherein said vessel is a vein.	Col. 2, line 22.
80. The method according to claim 78, wherein said pressure is sufficient to at least distend said vessel.	Col. 5, lines 19-23.
81. The method according to claim 78, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
82. The method according to claim 78, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
83. The method according to claim 78, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
84. The method of claim 78 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
85. The method of claim 78 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
86. The method of claim 78 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
87. The method of claim 86 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-12.
88. The method of claim 81 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
89. The method of claim 88 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Amended / New Claim	Support in Patent Disclosure
90. A method of locally administering an active agent to a host, said method comprising: retroinfusing a fluid into a vascular vessel of said host under conditions sufficient to at least distend said vessel, which distention facilitates the transport of said agent through the wall of said vessel so that said agent is locally administered to said host.	Col. 5, lines 19-23; Col. 1, line 66 – Col. 2, line 2.
91. The method according to claim 90, wherein said vessel is a vein.	Col. 2, line 22.
92. The method according to claim 90, wherein said pressure is sufficient to disrupt said vessel.	Col. 5, lines 35-36.
93. The method according to claim 90, wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.	Col. 7, lines 52 and 53.
94. The method according to claim 90, wherein said method further comprises producing inflammation in said vessel.	Col. 4, lines 62-64.
95. The method of claim 90 wherein said vessel is an artery.	Col. 3, line 18.

Amended / New Claim	Support in Patent Disclosure
96. The method of claim 92 wherein said vessel is a vein, and said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.	Col. 7, lines 1-3.
97. The method of claim 90 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.
98. The method of claim 97 wherein at least one upstream branch of said vessel is occluded.	Col. 7, lines 9-13.
99. The method of claim 92, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.	Col. 3, lines 42-54.

Amended / New Claim	Support in Patent Disclosure
100. The method of claim 99, wherein said vessel is a vein, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.	Col. 7, lines 1-3.

Respectfully submitted,

Orrick, Herrington & Sutcliffe LLP

Dated: Feb. 3, 2004

By _____
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Patent
Dkt. 13854.4004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Application of: Paul G. Yock, et al. Serial No.: Not yet Assigned, Reissue of U.S. Patent No. 6,346,098 B1 Filed: Herewith For: METHODS AND KITS FOR LOCALLY ADMINISTERING AN ACTIVE AGENT TO AN INTERSTITIAL SPACE OF A HOST	Group Art Unit: Not Yet Assigned Examiner: Not yet assigned Reissue Application of U.S. Patent No. 6,346,098 B1

JOINT DECLARATION OF PAUL G. YOCK, ALI H. HASSAN, ALAN CHING YEUN YEUNG, ANDREW CARTER, MEHRDAD REZAEE, NIALL HERITY, SIDNEY LO, AND PETER J. FITZGERALD UNDER 37 C.F.R. 1.175

We, Paul G. Yock, Ali H. Hassan, Alan Ching Yeun Yeung, Andrew Carter, Mehrdad Rezaee, Niall Herity, Sidney Lo, and Peter J. Fitzgerald jointly declare:

1. Each of our residence address, mailing address, and countries of citizenship are stated below next to our names.

CERTIFICATE OF MAILING
(37 C.F.R. §1.8

I hereby certify, pursuant to 37 CFR §1.8, that I have reasonable basis to expect that that this paper or fee (along with any referred to as being attached or enclosed) would be mailed or transmitted on or before the date indicated with the United States Postal Service with sufficient postage as first class mail on the date shown below in an envelope addressed to Mail Stop Reissue, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Signature of Person Mailing Paper

2. We believe that we are the original, first, and joint inventors of the subject matter described and claimed in United States Patent No. 6,346,098 B1 (hereinafter "the '098 Patent"), granted on February 12, 2002, and for which a reissue patent is sought on the invention entitled "Methods and Kits for Locally Administering an Active Agent to an Interstitial Space of a Host," the specification of which is submitted concurrently with this Declaration.

3. We do not know and do not believe that the invention was ever known in the United States of America before our invention thereof.

4. We believe that the '098 Patent may be partly inoperative or invalid by reason of the patentee claiming more or less than patentee had the right to claim in the patent.

5. This application is, in part, a broadening reissue application, and that an explanation of the nature of the broadening is set forth below.

6. At least one error in the original claims of the '098 Patent upon which reissue is based is described below.

7. The original claims of the '098 Patent each recited a method of locally administering an active agent to a host, but that several embodiments of the methods described in the '098 Patent, for which we are rightfully entitled to coverage by the claims of the '098 Patent, were not recited in the original claims, including the following (which are recited in new dependent claims 20-36):

a. The method recited in original claim 1 wherein said agent comprises cells.

b. The method recited in original claim 1 wherein said agent is a biological agent selected from the group consisting of peptides, proteins, nucleic acids, lipids, polysaccharides, and mimetics thereof.

c. The method recited in original claim 1, wherein said agent comprises therapeutic nucleic acids.

d. The method recited in original claim 1, wherein the agent comprises therapeutic nucleic acids, and wherein the therapeutic nucleic acids comprise at least one gene.

e. The method recited in original claim 1, wherein said agent comprises a dye or an imaging agent.

f. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 50 mm Hg.

g. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 60 mm Hg.

h. The method recited in original claim 1, wherein said retroinfusion is performed at a pressure of at least 1000 mm Hg.

i. The method recited in original claim 5, wherein the energy administered is selected from the group consisting of ultrasound, heat, electroporation and radio frequency energy.

j. The method recited in original claim 3, wherein said stress is chemical stress.

k. The method recited in original claim 1, wherein said vessel is an artery.

l. The method recited in original claim 2, wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruptions in the venous branches.

m. The method recited in original claim 1, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

n. The method recited in original claim 1 wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent, and wherein at least one upstream branch of said vessel is occluded.

o. The method recited in original claim 2, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site of administration of said agent.

p. The method recited in original claim 2, wherein said agent is retroinfused through a catheter having an occlusion device downstream of the site

of administration of said agent, and wherein said retroinfusion comprises disruption of venous branches upstream of the site of administration for said agent to enter an interstitial space of said host through the disruption in the venous branches.

q. The method recited in original claim 1, wherein said pressure is sufficient to at least distend said vessel.

8. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 7 and 7.a. through 7.q. are corrected by the inclusion of new claims 20 through 36, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, one of embodiments listed in paragraphs 7.a. through 7.q. that was not recited in the original claims of the '098 Patent.

9. The original claims of the '098 Patent, including independent claims 1, 8, and 13, each recite a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing said agent into a vascular vessel (claim 1) or vein (claims 8 and 13), whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing a fluid into a vascular vessel or vein followed by retroinfusing the agent, and, accordingly, that the claims thereof are insufficient because they are unnecessarily limiting.

10. The insufficiency of the original claims of the '098 Patent set forth in the paragraph 9 is corrected by the inclusion of new claims 37 through 55, each of which recites a

method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent, thereby presenting claims that are broader in this respect than the original claims of the '098 Patent.

11. Original claim 7 of the '098 Patent recites a method of locally administering an active agent to a host comprising, *inter alia*, administering an agent at a pressure sufficient to produce at least a mechanical stress on said vessel, whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host, and, accordingly, that the claims thereof are insufficient because they do not recite the foregoing methodology.

12. The insufficiency of the original claims of the '098 Patent set forth in the paragraph 11 is corrected by the inclusion of new claims 56 through 66, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

13. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 9 and 11 are further corrected by the inclusion of new claims 78 through 89, each of which

recites a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent – thereby presenting claims that are broader in this respect than the original claims of the '098 Patent – and each of which further recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vascular vessel of the host under conditions sufficient to produce at least a mechanical stress on the vessel, which stress facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

14. Original claim 13 of the '098 Patent recites a method of locally administering an active agent to a host comprising, *inter alia*, administering an agent at a pressure sufficient to at least distend a vein of the host, whereas the method of locally administering an active agent of the invention described in the '098 Patent may be practiced by retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension facilitates the transport of the agent through the wall of the vein so that the agent is locally administered to the host, and, accordingly, that the claims thereof are insufficient because they do not recite the foregoing methodology.

15. The insufficiency of the original claims of the '098 Patent set forth in paragraph 14 is corrected by the inclusion of new claims 67 through 77, each of which recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension

facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

16. The insufficiencies of the original claims of the '098 Patent set forth in paragraphs 9 and 14 are further corrected by the inclusion of new claims 90 through 100, each of which recites a method of locally administrating an active agent to a host comprising, *inter alia*, retroinfusing a fluid into a vascular vessel or vein to facilitate transport of an agent followed by retroinfusing the agent – thereby presenting claims that are broader in this respect than the original claims of the '098 Patent – and each of which further recites a method of locally administering an active agent to a host comprising, *inter alia*, retroinfusing an agent into a vein of the host under conditions sufficient to at least distend the vein, which distension facilitates the transport of the agent through the wall of the vessel so that the agent is locally administered to the host.

17. The insufficiencies in the original claims of the '098 Patent identified in paragraphs 7, 7.a.-7.q., 9, 11, and 14 arose, occurred or resulted from the fact that we and our attorneys failed to communicate adequately concerning the preparation of claims and prosecution of the application that issued as the '098 patent, and that our attorneys failed to appreciate the full scope of the invention and that the original claims would possibly preclude coverage of embodiments of the invention that are disclosed and supported by the patent specification, which embodiments are within a scope of coverage to which we are rightfully entitled.

18. Original claim 8 included recitation of "retroinfusing said agent into a vein of said host under conditions sufficient to produce a disruption in said vessel," whereas the term "vessel" should have been "vein" in order to properly reflect its antecedent.

19. Original claim 11 included recitation of a method that produces "inflamation" [sic] in said "vascular vessel," whereas it should have recited "inflammation in said vein".

20. Original claim 15 included recitation of pressure sufficient to produce a disruption "on" said vein, whereas it should have recited pressure sufficient to produce a disruption "in" said vein.

21. Original claim 19 included recitation of a method that produces "inflamation" [sic] in said "vascular vessel," whereas it should have recited "inflammation in said vein".

22. Each of claims 8, 11, 15, and 19 are amended in the Preliminary Amendment to correct the formal errors set forth in the preceding four paragraphs.

23. All of the aforementioned errors in the original patent that are being corrected in the reissue application up to the time of filing of this declaration arose without any deceptive intention on the part of any of us.

24. Each of us has reviewed and understands the contents of the above-identified application for Patent Reissue and the Preliminary Amendment filed herewith.

25. Each of us acknowledges the duty to disclose information which is material to the examination of this Application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a).

26. All statements made herein of our own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like may jeopardize the validity of this application for reissue or any patent issuing thereon.

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Lo S 7 Atlas Way Beaumont Hills 2155	(02) 9629 9065		
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Lo S 11 Railway St Chatswood 2067	(02) 9410 2085		
Lo S 21 Ryde St Epping 2121	(02) 9617 0183		
Lo S 110 Hudson St Hurstville 2220	(02) 9594 5965		
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Lo S 2 Anthony St Yagoona 2199	(02) 9708 3034		
Lo S & D 4a Balmoral St Waitara 2077	(02) 9989 8663		
Lo S & K 10 Wright St Hurstville 2220	(02) 9585 1668		
Lo S C 7 Hampstead Rd Homebush West 2140	(02) 9764 2238		
Lo S C 8 Torwood St Sans Souci 2219	(02) 9529 6223		
Lo S C M 2 Neutral Rd Hornsby 2077 2 Neutral Rd Hornsby 2077	(02) 9482 3185		
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Lo S H 5 B Mount St Hunters Hill 2110	(02) 9816 2635		
Lo S K 37 Phelps St Canley Vale 2166	(02) 9726 3471		
Lo S K 2 Thurlow St Riverwood 2210	(02) 9584 8238		
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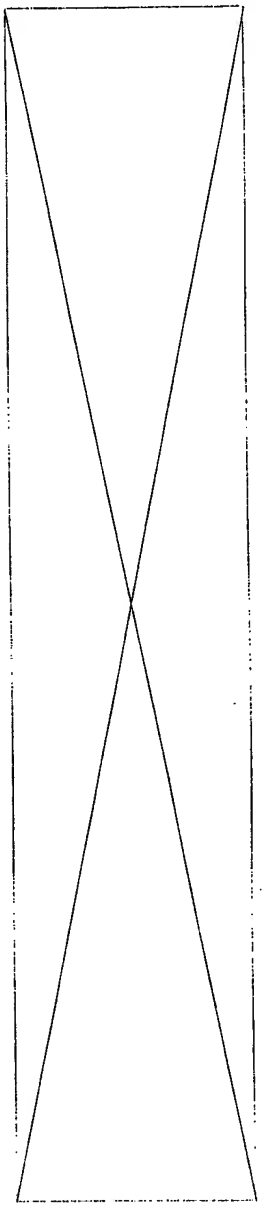

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